# United States Patent [19]

**Braden**

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[54] **METHOD AND APPARATUS FOR FORMING DROPLETS AND MICROCAPSULES**


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[73] Assignee: **Damon Biotech, Inc.**, Needham Heights, Mass.



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[22] Filed: **Apr. 30, 1986**

[51] **Int. Cl.**[4] ..... **A61K 9/62**; B01J 13/02; B28B 1/54

[52] **U.S. Cl.** ..... **264/4.3**; 264/4; 424/93; 424/455; 424/461; 425/5; 425/804

[58] **Field of Search** ..... 264/4, 4.3; 425/5, 804; 424/455, 461



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*Primary Examiner*—Richard D. Lovering
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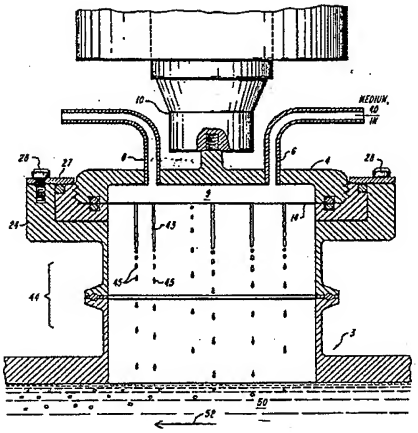
[57] **ABSTRACT**

A method and apparatus for forming microcapsules from a fluid medium containing living culture material by the atomization of the medium and the treatment of the atomized droplets with a treatment fluid. A medium under pressure enters a chamber having a wall with a plurality of orifices formed therein. A vibrator vibrates the chamber. As the medium passes through the orifices the exit stream vibrates and forms small droplets. The droplets fall into a collection vessel on the other side of the wall, which contains treatment fluid for hardening the droplets into microcapsules. A flow of treatment fluid may be maintained through the collection vessel to prevent clumping of the droplets and to transport the hardened microcapsules for harvesting. Preferred operating pressures, orifice size and chamber configuration are shown.


**16 Claims, 3 Drawing Figures**



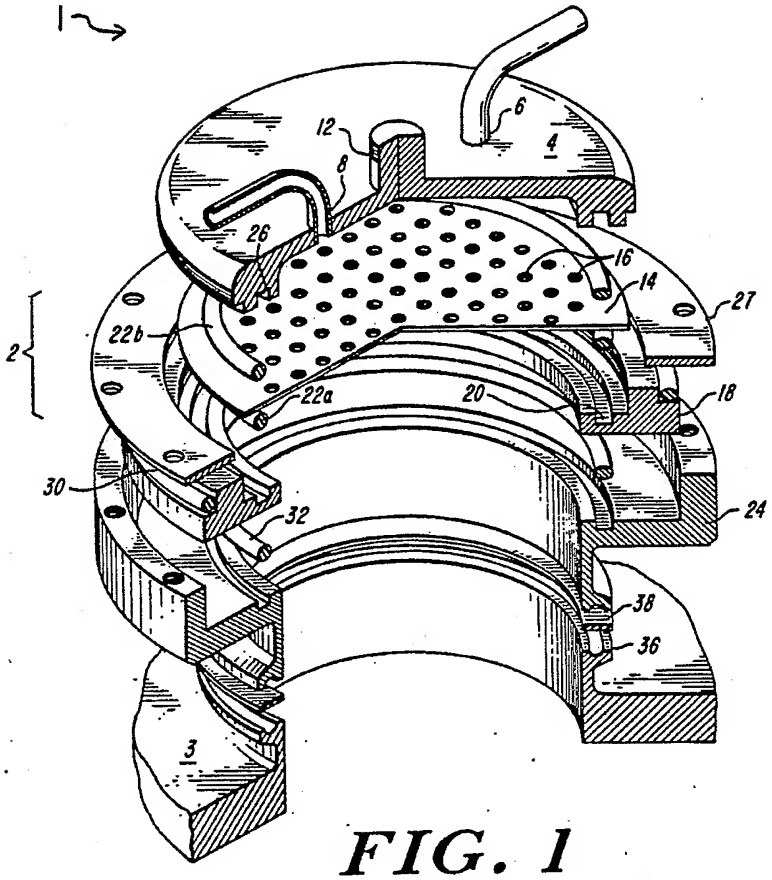



FIG. 1

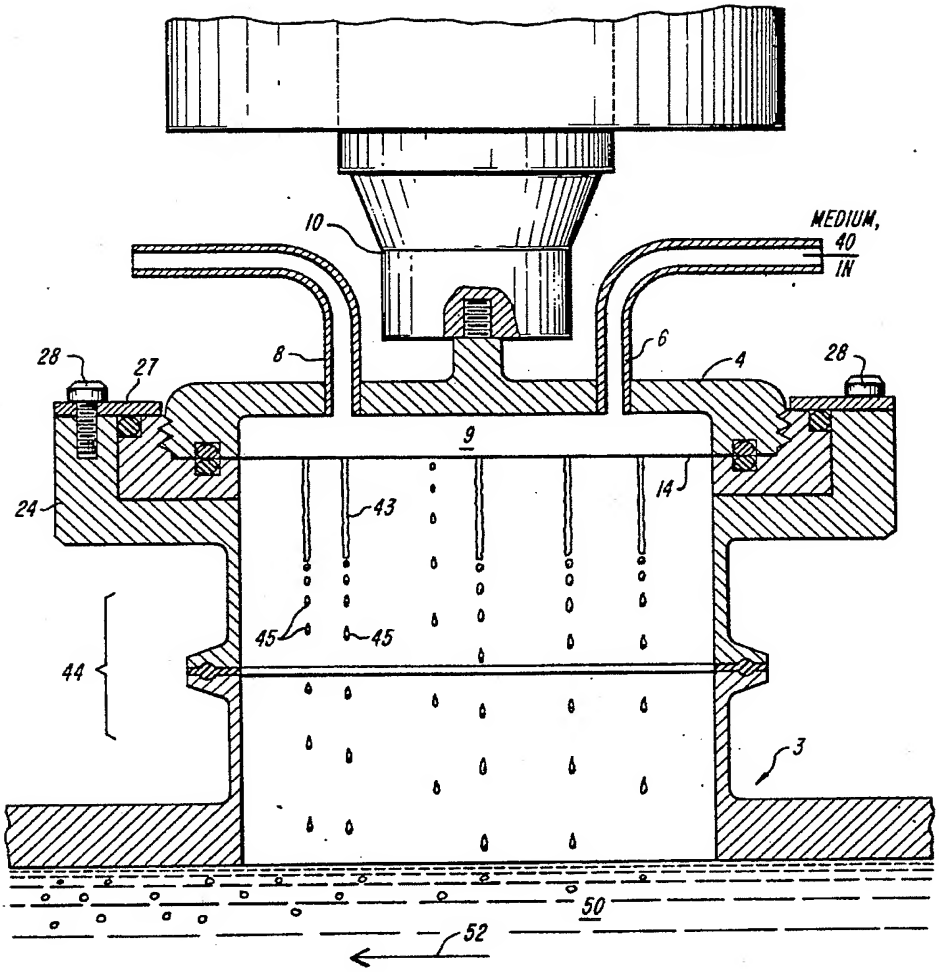



FIG. 2

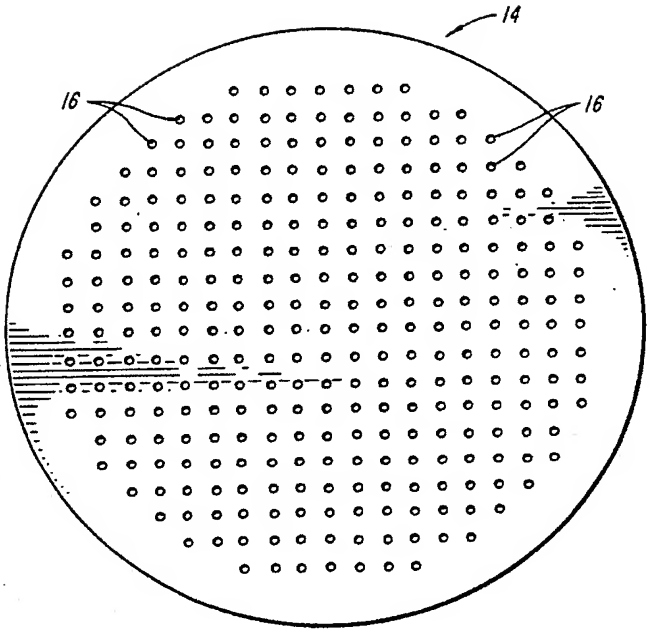



FIG. 3

# METHOD AND APPARATUS FOR FORMING DROPLETS AND MICROCAPSULES

## TECHNICAL FIELD

The present invention relates to the production of small droplets from a fluid medium, and more particularly to the production of such droplets from a culture medium, and the treatment thereof with a second fluid so as to form microcapsules.

The encapsulation of biological material has become a valuable tool in the fields of microbiology, genetic engineering, immunization, and the medical treatment of tissue. Such encapsulation involves the formation of droplets containing substances such as micro-organisms or live cell culture material, and the treatment of the droplets to form capsules thereof without injury of the encapsulated material. An example of this general technique is shown in U.S. Pat. No. 4,352,883, the disclosure of which is incorporated herein by reference.

One apparatus for the formation of such encapsulated material in a production line process is shown in U.S. Pat. No. 4,386,895, of Lester A. Sodickson. In that apparatus, a reservoir of biological medium is centrally located and surrounded by a reservoir of a gelling or hardening agent. The central reservoir rotates, forcing the medium through bundles of hollow outflow needles, similar to hypodermic needles, spaced about its periphery. As the medium flows out through the needles, it is atomized and received in the outer reservoir, where the atomized droplets of medium gel and harden into microcapsules. The inner diameter of the needles is chosen, in relation to the viscosity and other properties of the medium, so as to form droplets which are small enough to not disintegrate upon ejection into the treating agent of the outer reservoir. It is also possible to eject the atomized medium into a gas transport flow, or to have an impinging circumferential gas jet to facilitate the atomization process. One production line system currently employed produces droplets having a diameter of 600 microns with a size distribution of 200–300 microns above and below that size.

## OBJECTS AND SUMMARY OF INVENTION

It is an object of the present invention to provide an apparatus and method for the production of microcapsules at a high production rate.

It is another object of the invention to provide an apparatus and method for the production of microcapsules having a substantially uniform and small size.

It is another object of the invention to provide an apparatus and method for the production of microcapsules in which atomized droplets are produced while avoiding clumping of the droplets.

It is another object of the invention to provide an apparatus and method for the production of microcapsules in which atomized droplets are delivered to a treatment fluid and in which the droplets are formed of a size sufficiently small to avoid disintegration thereof on contact with the treatment fluid.

It is another object of the invention to provide an apparatus and method for the production of microcapsules which substantially avoids injury to biological growth material encapsulated therein.

These and other objects of the invention are realized in a method and apparatus for forming microcapsules from a fluid medium by the atomization of the medium and the treatment of the atomized droplets with a treatment fluid. The medium under pressure enters a chamber having a wall with a plurality of orifices formed therein. A vibrator vibrates the chamber, and the medium passes through the orifices, forming small droplets. The droplets fall into a collection vessel containing treatment fluid on the other side of the wall. Preferably, the pressure in the first chamber is selected to optimize the rate of droplet formation. A flow of treatment fluid may be maintained through the collection vessel to prevent clumping of the droplets and to transport the hardened microcapsules to a separation station.



## BRIEF DESCRIPTION OF THE DRAWINGS

These and other features of the invention will be understood by reference to the figures, in which:

FIG. **1** shows a perspective exploded view of a presently preferred embodiment of apparatus according to the invention;

FIG. **2** shows a section of the assembled apparatus of FIG. **1**; and

FIG. **3** shows a top view of the orifice member of the embodiment of FIGS. **1** and **2**.

## DETAILED DESCRIPTION

FIG. **1** shows an exploded perspective view of an apparatus **1** for the production of droplets from a biological medium according to a presently preferred embodiment of the invention. A supply chamber **2** receives a flow of the medium and forms droplets which fall into a collection vessel **3**. Supply chamber **2** includes a cap member **4** having an inlet port **6**, for providing a flow of the medium, and an outlet port **8**. Outlet port **8** serves as a bleeder for trapped air, and is useful in cleaning the apparatus. A vibrator **10** (shown in FIG. **2**) attaches to the cap via a coupling **12**. Sealed across a lower portion of the cap and forming a wall thereof so as to define the supply chamber is an orifice member **14** having a plurality of holes **16** formed therein.

In the preferred embodiment, the holes **16** have a uniform diameter of approximately 300 microns, and are formed on a grid pattern with a spacing of approximately 5 millimeters. Preferably, the orifice member is sheet titanium, approximately 0.25 millimeters thick, or is made of other hard durable material. Thus, a circular orifice member having a diameter of 10 centimeters, may have several hundred or more holes **16**. Preferably the holes are chemically etched. Alternatively, they may be formed by vaporization of the material therein with a laser drilling apparatus. A collar **18** having an annular groove **20** therein for receiving an O-ring **22***a* is fitted to the cap **4** for securing the orifice member in position. A second O-ring **22***b*, fitted in a similar groove **26** in the cap, provides a seal on the opposite side of the orifice member.

In this manner, member **14** is removably mounted in the cap, and can be conveniently interchanged with orifice members having different size holes for forming droplets of a different diameter, or for use with a medium of different viscosity. In the example discussed below, a hole size of approximately one-half of the desired droplet diameter has been found to yield excellent results.

The entire supply chamber structure consisting of the collar **18**, orifice member **14**, and cap **4** mount as a unit on a vessel platform **24** via annular flange **27** secured by cap screws **28** (shown in FIG. **2**). Supply chamber assembly **2** is sealed against the platform **24** with O-rings

30, 32 nested in grooves formed in the corresponding structures. The various housing pieces **4,18,24** are preferably formed of a surgical grade stainless steel such as a 316L material, and are finished, for example with a 240 grit abrasive followed by an electropolishing finish operation. The gaskets ***22a,22b,30,32*** are preferably formed of an inert, non-bleeding material of the type used for pressure seals, for example the fluoroelastomer material sold commercially under the trade name Viton and widely used in the biological industry, or a silicone elastomer. Below the platform **24** is a collection vessel **3** to which the vessel platform **24** is connected via a triclamp which fits about a bevelled flange area **36** thereof. A gasket **38** seals the connection.

As shown in FIG. **1**, the supply chamber **2** with its attached vibration unit is adapted for fitting over a vessel, with a fitting of a type conventionally used in a biological culture system. The vessel **3** serves as an encapsulating vessel for receiving the formed droplets and treating them with a hardening treatment fluid. The vibration generator **10** may be a piezoelectric driving unit. One suitable unit is sold by the Wilcoxon Company as their model number F7/F4/Z7. Other piezo units are readily available commercially, and other types of drive units, such as an electromagnetic driver or a motor driven eccentric cam vibrator may also be used.

Turning now to FIG. **2**, there is shown a perspective cross section of the apparatus of FIG. **1**. Identical parts are identically numbered therein. As shown in FIG. **2**, a pressurized flow of the medium **40** which is to be encapsulated is provided through the inlet port **6** into the relatively shallow interior space **9** of the supply chamber (**2** of FIG. **1**). In the preferred embodiment, space **9** has a depth between its roof and the orifice member of approximately 6 millimeters. There is thus a negligible hydrostatic pressure gradient, and the cap member is strongly coupled through the chamber to the orifice member **14**, which is a thin diaphragm-like member. Medium **40** is driven through the orifice member **14** in part by pressure and in part by the mechanical transport action of the sonic vibration applied to the chamber by vibrator **10**, forming thin columns **43**. The columns **43** break up into droplets **45** having a substantially uniform diameter.

When the medium passes through the member **14**, standing wave in the columns of medium atomize the material into droplets **45**. The atomized droplets **45** descend through the neck **44** defined by vessel platform **24** and the vessel coupling, into the collection vessel **3** where they contact a body of treatment fluid **50** such as the calcium chloride or other divalent metal hardening solution, as described in the aforesaid U.S. Pat. No. 4,386,895. The neck region **44** between the member **14** and the surface of a body of treatment fluid **50** in the collection vessel is maintained at a slight supra-atmospheric pressure by a vent, and has a vertical dimension in the range of 3–5 cm, which is just sufficient to allow atomizing breakup of the extruded column-like jets **43** of medium **40**. Collection vessel **3** may comprise a portion of a circulation loop, wherein the fluid **50** is carried along a flow path indicated by arrow **52** to a filter or other separator for harvesting, so that the hardened microcapsules are continuously removed from the collection fluid.

In a preferred embodiment, vessel **3** is a stirred reactor vessel with an extremely low height to diameter ratio relative to conventional reactors. Multiple filter elements result in a high flow rate of treatment fluid through the vessel while decreasing mechanical damage to the capsules during solution removal. The supra-atmospheric pressure prevents the entry of external contaminants into the system.

FIG. **3** is a top view of the orifice member **14** of FIG. **1**. As shown, orifice member **14** comprises a thin planar portion having a plurality of holes or orifices **16** evenly spaced throughout a central region thereof. The spacing between holes **16** is selected to be small enough to provide a large number of holes to optimize through-flow of material, yet dispersed enough to prevent clumping of the atomized droplets which have passed therethrough. The diameter of the holes **16** is selected to provide droplets of the desired size, and will vary somewhat depending upon the viscosity of the medium **40**, the drive frequency of vibrator **10**, and the operating pressure difference of the apparatus across the orifice member **14**. The operating pressure must be low enough to avoid damage to the viable material of the medium **40**.

One prototype apparatus having a structure as shown in FIG. **1** was operated with a 1.6% aqueous sodium alginate solution having a viscosity of 80 centipoise. The apparatus had a supply chamber and orifice member diameter of approximately 9 cm., and was attached to a 10 cm port of a collection vessel. Cell medium was supplied to the inlet at a pressure of up to approximately 2.7 atmospheres by pressurizing a supply tank with nitrogen to force the fluid through a high pressure delivery tube to inlet **6**.

Under these conditions, the apparatus converted the cell medium to droplets at a rate of between 5 and 10 millilitres/minute per orifice. The vibrational drive was supplied by a piezoelectric vibrator operated at a 1000 Hz frequency with a sine wave input having a drive power of approximately 100 watts. The orifice size was 300 microns. The droplets so produced had a diameter of 600 microns, with over 90% of the droplets lying between 550 and 650 microns. These characteristics constitute a significant improvement, both as to droplet uniformity and rate of droplet production. For example, an orifice member in a ten centimeter diameter supply chamber with 100–200 orifices converts between one-half and two liters/minute of medium into microcapsules.

A preferred apparatus for the invention having been thus disclosed, other variations of apparatus, and of methods of practicing according to the invention will occur to those skilled in the art, and all such variations are intended to be within the scope of the invention, as defined by the following claims.

What is claimed is:

**1**. Apparatus for forming microcapsules of a desired size from a fluid medium containing living culture material by the atomization of the medium, such apparatus comprising:

a flow chamber for flowing the medium therethrough and including

(a) a flow cap, having an inlet port and

(b) a wall member having first and second opposing sides, said wall member being attached to the cap such that the cap and said first side define said chamber, said wall also having a plurality of orifices formed therethrough;

pressure means, for pressurizing the flow chamber to drive the medium through the orifices;

vibration means for vibrating the chamber to atomize the medium flowing through the orifices; and

means for coupling the apparatus to a collection vessel on the second side of the wall so as to deliver to the collection vessel said atomizing flow.

2. Apparatus according to claim 1, wherein the orifices have a diameter in the range of approximately 100–500 microns.

3. Apparatus according to claim 2, wherein the pressure means includes means for providing pressure in the range of approximately 1 to 4 atmospheres.

4. Apparatus according to claim 3, wherein the wall member is a perforated diaphragm.

5. Apparatus according to claim 4, further including a collection vessel and means for flowing treatment fluid through the collection vessel.

6. Apparatus according to claim 1, wherein the wall member is a perforated diaphragm.

7. Apparatus according to claim 6, wherein the cap and wall define a roof and a floor, respectively, of the chamber and wherein the distance between the roof and the floor is less than approximately one-quarter of the diameter of the diaphragm.

8. A method for forming microcapsules of a fluid medium containing living culture material by the atomization of the medium and the treatment of atomized droplets thereof with a treatment fluid, such method comprising the steps of:

flowing the medium through an inlet port into a flow chamber having a flow cap and a wall member having first and second opposing sides, said wall member being attached to the cap such that the cap and said first side define said chamber, said wall also having a plurality of orifices formed therethrough;

providing pressure in said chamber to drive the medium through the orifices,

vibrating the chamber to atomize the medium driven through the orifices, and

receiving said atomized flow in a vessel of the treatment fluid on the second side of the wall.

9. The method of claim 8, wherein the orifices have a diameter in the range of approximately 100–500 microns.

10. The method of claim 9, wherein the wall member is a perforated diaphragm.

11. The method of claim 10, further including the step of flowing treatment fluid through the collection vessel.

12. The method of claim 11, wherein the step of providing pressure includes providing pressure in the range of approximately 1 to 4 atmospheres.

13. Apparatus for the production of sub-millimeter droplets from a fluid medium containing living culture material, such apparatus comprising:

a shallow cap having a roof portion,

a vibrator affixed to the cap,

an orifice member affixed to the cap opposite the roof portion so as to define, together with the cap, a closed chamber, said orifice member including one or more orifices therethrough of a diameter functionally related to a desired droplet diameter,

spacing means for providing a free-fall space below said orifice member, and

pressure means for pressurizing the chamber so as to drive the medium therein as a fluid stream through the orifices whereby the droplets are produced by vibration of the fluid stream in the free fall space.

14. Apparatus according to claim 13 wherein the orifice member is removably and replaceably affixed to the cap.

15. Apparatus according to claim 14, further including a treatment vessel, coupled to the spacing means, for receiving said droplets and treating them with a treatment fluid.

16. Apparatus according to claim 15, wherein the diameter of the orifices is approximately one-half of the desired droplet diameter.

* * * * *

US005472648A

# United States Patent [19]

Alisch et al.

[11] Patent Number: 5,472,648

[45] Date of Patent: Dec. 5, 1995

[54] **PROCESS AND PLANT FOR THE PRODUCTION OF SPHERICAL ALGINATE PELLETS**

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[73] Assignee: **Nukem GmbH**, Alzenau, Germany

[21] Appl. No.: **185,893**

[22] PCT Filed: **Jul. 22, 1992**

[86] PCT No.: **PCT/EP92/01670**

§ 371 Date: **Jun. 13, 1994**

§ 102(e) Date: **Jun. 13, 1994**

[87] PCT Pub. No.: **WO93/02785**

PCT Pub. Date: **Feb. 18, 1993**

[30] **Foreign Application Priority Data**

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[51] **Int. Cl.**[6] ..... **B29B 9/10**

[52] **U.S. Cl.** ..... **264/9**; 264/14; 425/6; 425/10

[58] **Field of Search** ..... 264/4, 5, 9, 14; 425/5, 6, 10

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*Primary Examiner*—Mary Lynn Theisen
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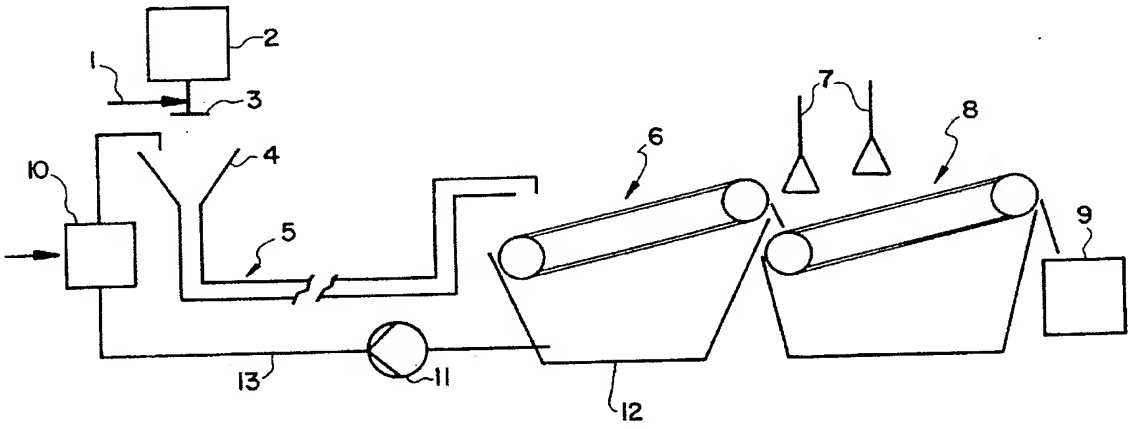
[57] **ABSTRACT**

Proposed is a process for the production of spherical alginate pellets from drops of alginate solution delivered by a nozzle, the drops being solidified by dropping them into an ionic solution and subsequently removing the pellets and rinsing them. The alginate solution is converted into drops by vibrational stimuli, and the drops subsequently allowed to remain substantially free in the ionic solution until the required degree of solidification has been reached.

**12 Claims, 3 Drawing Sheets**



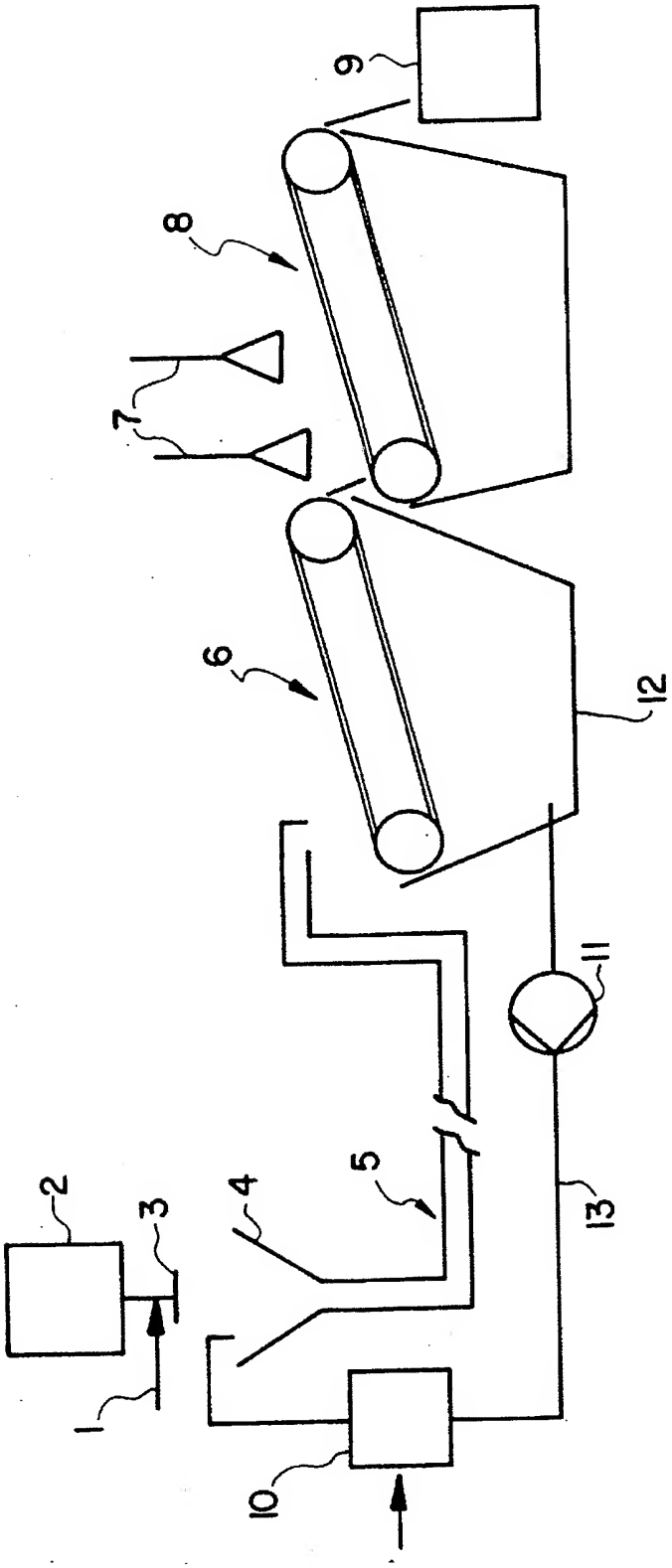



FIG. 1

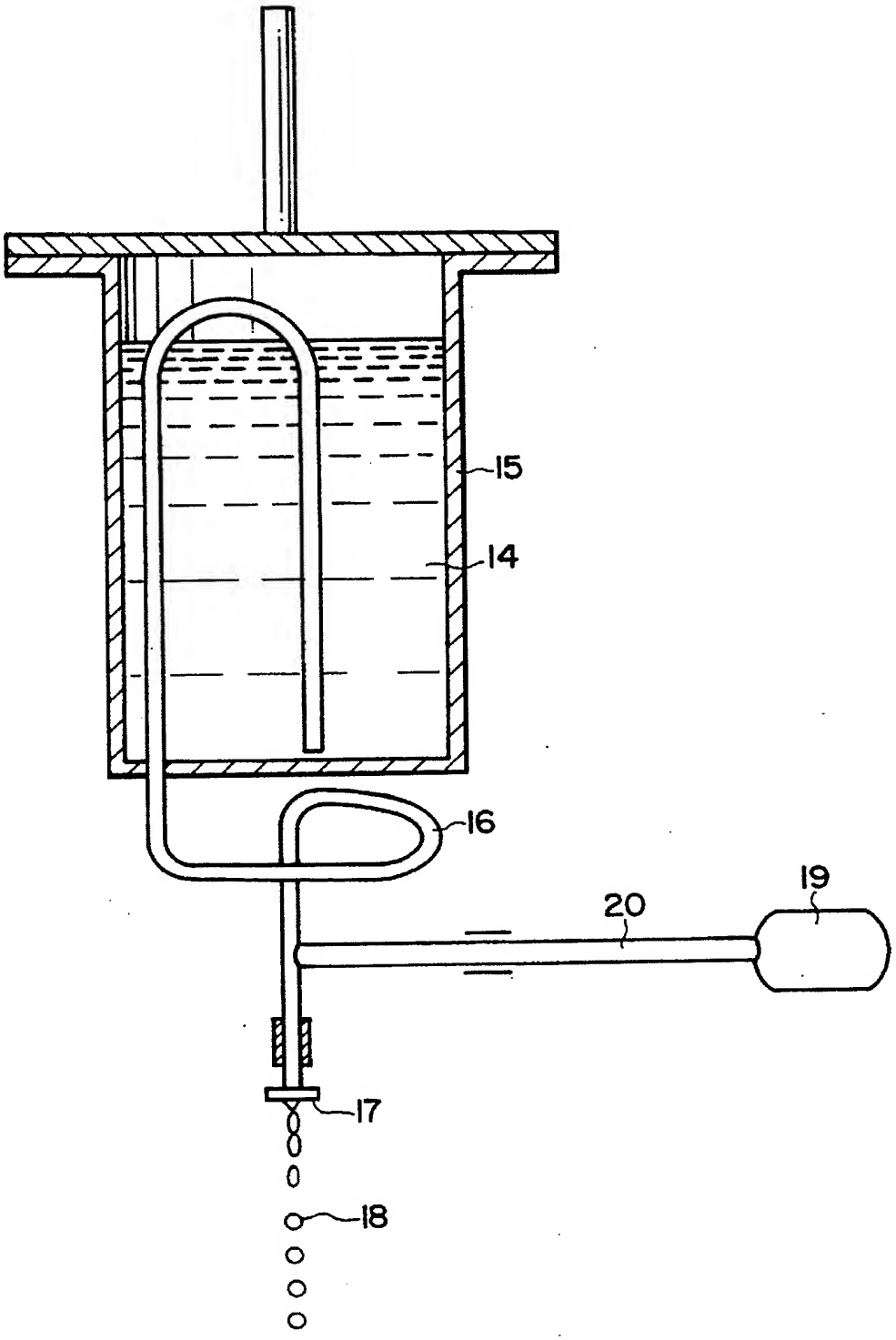



FIG. 2

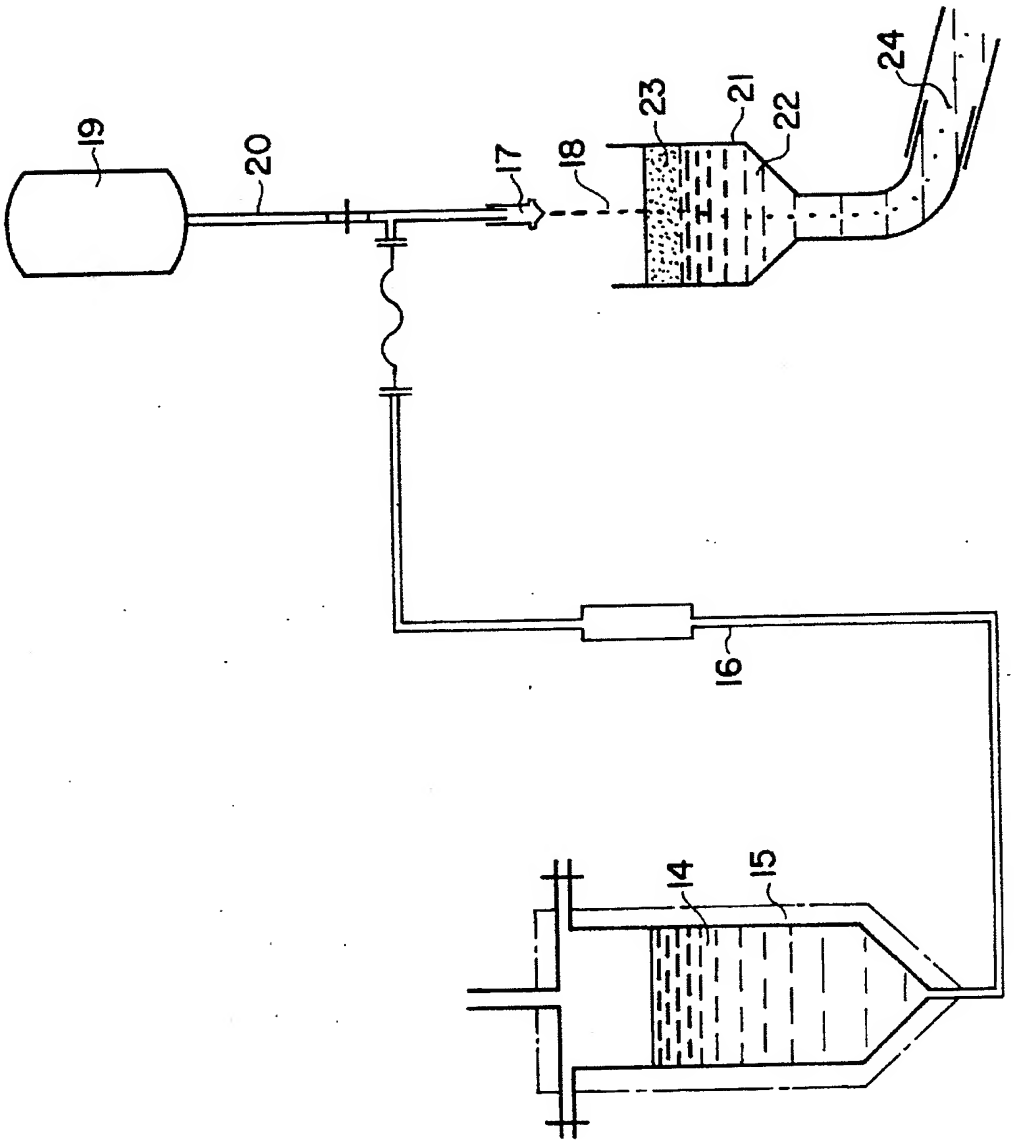



FIG. 3

# PROCESS AND PLANT FOR THE PRODUCTION OF SPHERICAL ALGINATE PELLETS

## BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention refers to a method for producing spherical alginate pellets from droplets of an alginate solution delivered from a nozzle, by consolidating the droplets by dropping them into an ion solution, preferably a calcium ion solution, and subsequently washing the alginate pellets removed from the ion solution. The invention further refers to an apparatus for producing spherical alginate pellets from droplets of an alginate solution, comprising a reservoir vessel for the alginate solution; at least one nozzle to which alginate solution can be fed as applicable via a feed line; a collection device, containing an ion solution, for the droplets falling from the nozzle; and at least one device for removing the alginate pellets from the collection device.

Alginate pellets are required, for example, as thickening agents in emulsions, in the cosmetics and food industries, for adhesives and finishes, or as base substances for elastic molding compounds in dentistry, for example. In use, however, the alginate pellets are either completely hardened or only surface-hardened.

Surface-hardened alginate pellets are required, for example, in the cosmetics industry, while completely hardened alginate pellets are required, for example, as supports for enzymes. In order for alginate pellets to be usable to the desired extent, they must be sufficiently pourable and have a narrow particle size spectrum. In particular, a uniform geometry (i.e. a spherical shape) should also be present.

2. Description of the Prior Art FR-A 2 645 439 has disclosed a method for producing spherical alginate pellets intended for the cosmetics industry, according to which an alginate solution is fed to a nozzle from which the alginate solution is delivered in droplet form, subsequently falling into a calcium ion solution. Located in the calcium ion solution is an endless-loop conveyor belt by which the droplets are collected and then transported out of the calcium ion solution.

Since there is no assurance that the droplets are surface-hardened to a sufficient extent as they fall through the calcium ion solution, the alginate pellets removed from the calcium ion solution by the conveyor belt are often flattened. Since the droplets form simply by dripping alginate solution out of the nozzle, a desirable narrow particle size spectrum also cannot be achieved.

## SUMMARY OF THE INVENTION

The underlying problem of the present invention is to develop a method and an apparatus of the aforesaid type for producing spherical alginate pellets in such a way that, among other effects, alginate pellets with a spherical geometry and a narrow particle size spectrum are obtained, and that hardening of the alginate pellets themselves can be adjusted in a controlled manner.

According to the invention, the problem is solved in terms of the method by the fact that the alginate solution is formed into drops by vibratory excitation, and that until they achieve the desired consolidation, the droplets are initially, until surface hardening occurs, substantially free to move in the ion solution. In this connection an "ion solution" is understood to mean an ionic solution whose metal ions combine with alginate to form a poorly soluble compound. Preferably the ion solution can be a calcium ion solution.



In contrast to the prior art, the alginate solution is not dripped, but rather formed into drops by the nozzle, which itself can be excited to vibrate. This is not, however, a mandatory feature. Instead vibratory excitation can also occur by exciting the alginate solution in a reservoir container or by acoustic irradiation of the alginate solution itself.

Regardless of the kind of vibratory excitation, however, it is essential that a constant frequency act on the alginate solution, with rotationally symmetrical constrictions being generated and reinforced in a stream of liquid leaving the nozzle, so that uniform disintegration into droplets, called "dropletization," occurs. This ensures that the droplets have identical or almost identical sizes, so that as a result, the alginate pellets produced have a narrow particle size spectrum.

While dropletization ensures the narrow particle size spectrum, the feature by which the droplets remain free to move for so long within a precipitation solution (i.e. the ion solution)—in other words can move freely without striking masses that are large by comparison with the alginate mass—guarantees that the droplets are not deformed while hardening, and that consequently the final geometry of the alginate pellets exhibits a spherical geometry. In this connection the residence time in the alginate solution can be adjusted in a controlled manner so that consolidation can be performed reproducibly.

According to a development of the invention, the droplets can fall under their own weight through an ion solution column until the desired consolidation occurs. It is also possible, however, to define the residence time of the droplets in the ion solution by means of the flow velocity of the solution in which the droplets are moving.

A further proposal of the invention worth emphasizing provides for the droplets, before contacting the precipitation solution, to be intercepted on a foam present thereon, which can have a thickness of, for example, 5–50 mm. The droplets are decelerated while falling through the foam, so that when they subsequently contact the surface of the precipitation solution, flattening of the alginate droplets is largely ruled out.

To reduce the surface tension of the precipitation solution even further, a surfactant or an organic solvent, preferably an alcohol such as ethanol, propanol, etc., can be added thereto.

An apparatus for producing alginate droplets is characterized by the fact that the apparatus for dropletizing the alginate solution delivered by the nozzle has a vibration exciter, and that the collection device has a liquid column of the ion solution of a length such that the droplets can be consolidated to the desired extent while flowing through the liquid column. A liquid column in this case is not necessarily to be understood as, for example, a tubular reactor (plug flow reactor) in the shape of a tube or hose containing the precipitation solution, with which the exact residence time of the alginate droplets or pellets in the precipitation solution can be adjusted and varied to the desired degree. The term "liquid column" very generally denotes a quantity of liquid which offers the alginate droplets dropping into the precipitation solution the opportunity not to come into contact with masses that are large by comparison with the alginate droplets before the desired hardening, especially surface hardening, has occurred. Thus a batch reactor with or without a stirrer (for complete hardening of the alginate pellets) can also be utilized.

A mechanical vibrator, magnetic-induction vibrator, pneumatic vibrator, piezoelectric converter, or electroacoustic converter can be used as the vibration exciter; the vibration exciter can act on the nozzle and/or on the feed line and/or on the reservoir container. It is also possible to acoustically irradiate the alginate solution directly, for example with an electroacoustic converter, or to excite it directly with a vibrating displacer or plunger, in order to dropletize the stream of alginate solution emerging from the nozzle into uniform droplets.

Preferably the ion solution, which is preferably a $CaCl_2$ solution, has a surfactant or organic solvent added to it in order to reduce the surface tension of the precipitation solution.

To greatly reduce the "impact" of the alginate droplets on the surface of the precipitation solution, a foam layer, which itself is a foamed solution of surfactant or organic solvent, can be formed on the ion solution. The height of this foam layer is preferably between 5 and 50 mm.

The frequency acting on the apparatus or the alginate solution must be kept constant during the production process, with excitation frequencies of between 50 and 20,000 Hz preferably being used. The viscosity of the alginate solution should be less than 200 mPaxs. Lastly, the diameter of the nozzle should fall in the range between 50 and 3000 μm.

With these parameters, spherical alginate pellets of uniform geometrical configuration with a narrow particle size spectrum can be generated; depending on frequency and nozzle diameter, alginate pellet diameters of between 100 and 4000 um can be achieved.

Further details, advantages, and features of the invention are evident not only from the Claims [and] the features evident from them—individually and/or in combination— but also from the description below of preferred exemplary embodiments presented in the drawings, in which:

## BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows a schematic depiction of an apparatus for producing spherical alginate pellets;

FIG. **2** shows a first exemplary embodiment of an apparatus for producing droplets of an alginate solution; and

FIG. **3** shows a second embodiment of an apparatus for producing droplets from an alginate solution.

## DESCRIPTION OF THE PREFERRED EMBODIMENT

In FIG. **1**, reference number (**1**) designates a system for feeding and metering an alginate solution that is delivered via a nozzle (**3**) into a collection device (**4**) which contains an ion solution, preferably in the form of 2% $CaCl_2$ in deionized water.

In order for the alginate solution delivered by the nozzle (**3**) to dropletize, i.e. in order to obtain alginate solution droplets of reproducible size, a vibration exciter system that is indicated purely schematically and given the reference number (**2**) is provided. This exciter system can act directly on the nozzle (**3**) and cause it to vibrate horizontally or vertically. It is also possible to impress vibrations on the feed line (**1**). Alternatively, it is possible to excite the alginate solution present in a reservoir container. Lastly, the stream of alginate solution leaving the nozzle (**3**) can also be acoustically irradiated.

Potential vibration exciters include magnetic-induction vibrators, mechanical vibrators, pneumatic vibrators, piezoelectric converters, and electroacoustic converters.

In the schematic depiction according to FIG. **1**, the alginate droplets fall from the collection device (**4**)—in which a foam layer of a surfactant solution, with a height of, for example, 5–50 mm, can be present on the ion solution—through a tubular reactor (**5**); inside the tubular reactor (**5**), the alginate droplets are to be free to move at least until surface consolidation has occurred. Under these conditions the alginate droplets have the desired spherical geometry, so that a collision with other alginate droplets or pellets, or with the walls of the tubular reactor (**5**), will cause no further deformation.

After leaving the tubular reactor, the alginate pellets, consolidated to the desired degree, are delivered onto a traveling screen (**6**), from which the calcium chloride solution remaining on the alginate pellets drips off. From the traveling screen (**6**) the alginate pellets pass onto a traveling screen (**8**), on which they are washed using wash water nozzles (**7**). From the traveling screen (**8**) the alginate pellets are collected as finished products in a collection device (**9**), and then passed on to their desired application.

The ion solution flows through the tubular reactor (**5**) at a desired velocity. The residence time of the alginate droplets or pellets in the ion solution is determined by the velocity of the ion solution and the length of the tubular reactor, so that they can be consolidated reproducibly to the desired degree. The ion solution is conveyed by means of a pump (**11**) through a circuit which comprises a connection (**13**) from a collection container (**12**) present beneath the traveling screen (**6**) to the collection device (**4**). Also located in the connection or line (**13**) is a flow concentration controller (**10**) for the ion solution.

FIG. **2** depicts a section of an apparatus for producing spherical alginate pellets, specifically that with which droplets are produced from the alginate solution. The alginate solution (**14**) is located in a reservoir vessel (**15**) from which the alginate solution (**14**) is fed via a feed line (**16**) to a nozzle (**17**), from which the alginate solution (**14**) falls under its own weight in the form of droplets (**18**). It is evident that directly below the nozzle (**17**) the droplets have an elongated shape; after they have fallen a certain distance this changes into a spherical shape due to the surface tension of the alginate solution.

A vibration generator (**19**), which is connected directly or indirectly to the nozzle (**17**) via a rigid connection (**20**), generates a vibration which causes dropletization of the alginate solution leaving the nozzle (**17**), i.e. rotationally symmetrical constrictions are generated and reinforced in the stream of liquid leaving the nozzle (**17**), causing disintegration into uniform droplets.

Although according to the exemplary embodiment of FIG. **2** the alginate solution (**14**) is fed to the nozzle (**17**) by gravity, according to the exemplary embodiment of FIG. **3** a pressure delivery system is provided. Otherwise the configuration of FIG. **3** corresponds to that of FIG. **2**, and identical elements are therefore also given identical reference numbers.

Additionally depicted is a collection device (**21**) in which, for example, a calcium chloride solution is present or through which it flows. Located above the liquid level of the calcium chloride solution is a foam layer (**23**) of a surfactant solution, which "decelerates" the droplets (**18**). The resulting advantage is that when the droplets (**18**) strike the liquid

surface of the calcium chloride solution, undesired flattening is largely eliminated.

The droplets (18) that fall or are conveyed through the solution are initially consolidated externally by reaction with the calcium chloride solution, so that alginate pellets (24) of a desired consolidation are present within the chloride solution (22); as mentioned, consolidation depends on the residence time of the alginate pellets in the calcium chloride solution (22).

The reactor (21) containing the calcium chloride or precipitation solution can—as in the exemplary embodiment of FIG. 1—be a tubular reactor with which the exact residence time of the alginate pellets (24) in the precipitation solution can be adjusted by varying the reactor length and the flow velocity of the precipitation solution, thus generating alginate pellets (24) that [have] a desired consolidation, i.e. can be hardened only at the surface or completely hardened.

The reactor can also be a batch reactor which may possibly have a stirrer, especially if the alginate pellets (24) are to be completely hardened.

With regard to the precipitation solution, it should also be noted that a surfactant or organic solvent can be added to it in order to reduce the surface tension. As described with reference to FIG. 3, a foam of surfactant or organic solvent can also be present on the precipitation solution (22). It is also possible to take the precipitation solution (22) from a receiving device with an overflow channel.

The nozzle used to dropletize the alginate solution can be a full-flow nozzle made of various materials. It is also possible to use a nozzle plate, namely one with a plurality of nozzles.

The alginate solution used in the method according to the invention should have a viscosity less than 200 mPa×s. The excitation frequency with which the solution emerging from the nozzle is dropletized should be between 50 and 20,000 Hz. The nozzle diameter itself can lie in the range between 50 and 3000 µm. When these parameters are observed, alginate pellet diameters in the range between 100 and 4000 µm, with an almost exactly spherical shape, can be obtained. The respective alginate pellets produced under identical parameters have a very narrow particle size spectrum.

The examples below indicate further advantages and features of the invention, which—individually or in combination—are to be regarded as inventive.

## EXAMPLE 1

A reservoir vessel (15) contains an alginate solution that is fed to the nozzle (17) with a diameter of 280 µm, which in turn is caused to vibrate at a frequency of 2100 Hz. The dropletized alginate solution falls into a calcium ion solution, specifically into 2% CaCl2 in deionized water. The alginate droplets or pellets remain in the precipitation solution for 30 minutes, resulting in complete hardening. The diameter of the resulting spherical pellets is 500 µm, with a standard deviation of approximately 1%. No foam was present on the precipitation solution itself.

## EXAMPLE 2

To obtain surface-hardened alginate pellets, a tubular reactor containing a precipitation solution in the form of 0.35% $CaCl_2$ plus 0.05% surfactant and deionized water is used. The nozzle with which the alginate solution is dropletized has a diameter of 900 µm. The vibration frequency is 155 Hz. The alginate pellets remain in the precipitation solution for 1 minute. As a result, alginate pellets with a hardened surface and a diameter of 1700 µm are obtained. In this case as well, the standard deviation is 1%.

## EXAMPLE 3

Once again a tubular reactor is used, containing a precipitation solution with the following composition: 0.26% $CaCl_2$ plus 0.05% surfactant in deionized water. The nozzle used has a diameter of 1925 µm. The frequency is 50 Hz. A surfactant foam approximately 20 mm high is present on top of the precipitation solution. The alginate pellets remain in the precipitation solution for 1.5 minutes. As a result, surface-hardened alginate pellets with diameters of 3400 µm are obtained. Standard deviation is 1%.

## EXAMPLE 4

A processing sequence corresponding to that of Example 3 is performed, but instead of 0.05% surfactant, 8% isopropyl alcohol is added to the $CaCl_2$ solution. The alginate pellets produced in this manner also have the desired properties in terms of surface hardening and diameter (3400 µm with a standard deviation of 1%).

We claim:

1. Method for producing spherical alginate pellets from droplets of an alginate solution delivered from a nozzle, by consolidating the droplets by dropping them into an ion solution and subsequently washing the alginate pellets removed from the ion solution, wherein

the alginate solution is dropletized by vibratory excitation;

the droplets are substantially free to move in the ion solution until they achieve the desired consolidation; and

before contacting the ion solution, the droplets are decelerated by a foam present thereon, and/or the droplets fall into the ion solution whose surface tension has been reduced by a surfactant or an organic solvent.

2. Method according to claim 1 wherein the alginate solution is dropletized by vibratory excitation and the droplets are substantially free to move in the ion solution until they achieve the desired consolidation, the residence time of the droplets in the ion solution being dependent substantially on the flow velocity of the ion solution and the length of ion solution through which the droplets flow.

3. Method according to claim 1 wherein the droplets are substantially free to move in the ion solution at least until they achieve surface hardening.

4. Method according to claim 2 wherein the droplets are substantially free to move in the ion solution at least until they achieve surface hardening.

5. Method according to claim 1 wherein the droplets fall under their own weight through an ion solution column until the desired consolidation occurs.

6. Method according to one of claims 1–5 wherein the nozzle and/or the alginate solution and/or a reservoir container receiving the alginate solution and/or a feed line feeding the alginate solution to the nozzle is caused to vibrate.

7. Apparatus for producing spherical alginate pellets from droplets of an alginate solution (14), comprising a reservoir container (15) for the alginate solution; at least one nozzle (3, 17) to which alginate solution can be fed as applicable via a feed line (16, 20); a collection device (4, 21), containing an ion solution for the droplets falling from the nozzle; and at least one device for removing the alginate pellets from the

collection device (6, 7, 8, 9), wherein the apparatus for dropletizing the alginate solution (14) delivered by the nozzle (3, 17) has a vibration exciter (2, 19); and the collection device (4, 5, 21) is a tubular reactor through which the ion solution (22) can flow in an adjustable manner, with a liquid column such that the droplets (18) can be consolidated at least on their surfaces wile flowing through the liquid column.

8. Apparatus according to claim 7, wherein the vibration exciter is a mechanical or magnetic-induction vibrator, a pneumatic vibrator, a piezoelectric converter or electroacoustic converter, or a vibrating displacer/plunger.

9. Apparatus according to claim 7, wherein the vibration exciter (2, 19) acts on the nozzle (3, 17) and/or on the feed line (1, 16) and/or on the reservoir container (15) or on the interior of the nozzle.

10. Apparatus according to claim 8, wherein the vibration exciter (2, 19) acts on the nozzle (3, 17) and/or on the feed line (1, 16) and/or on the reservoir container (15) or on the interior of the nozzle.

11. Apparatus according to claim 7, further comprising a means by which the alginate solution (14) can be acoustically irradiated.

12. Apparatus according to one of claims 7–11 wherein the ion solution contains $Ca^{2+}$ ions or one or more other ion species that form a poorly soluble compound with alginate.

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